Application No.: 10/789,273 Docket No. ELN-002CPCN3

AMENDMENTS TO THE CLAIMS

1. **(Original)** A method for effecting improvement of cognition in a subject having a condition or disease related to Aβ, comprising administering to the subject an effective amount of an anti-Aβ antibody.

2. **(Original)** The method of Claim 1, wherein the subject is human.

3. **(Original)** The method of Claim 2, wherein the condition or disease is Alzheimer's disease, Down's syndrome, or mild cognitive impairment.

4. **(Original)** The method of Claim 3, wherein the disease is Alzheimer's disease.

5. **(Original)** The method of Claim 3, wherein the disease or condition is Down's syndrome.

6. **(Original)** The method of Claim 3, wherein the disease or condition is mild cognitive impairment.

7. **(Original)** The method of any one of Claims 1 - 6, wherein the antibody binds Aβ with an affinity of at least 10^{-9} M.

8. **(Original)** The method of any one of Claims 1 - 6, wherein the antibody binds Aβ with an affinity of at least 10^{-10} M.

9. **(Original)** The method of any one of Claims 1 - 8, wherein the antibody is a humanized or human antibody.

10. **(Original)** The method of Claim 9, wherein the antibody is a humanized 266 antibody, or an analog thereof.

11. **(Original)** The method of any one of Claims 1 - 10, wherein the anti-Aβ antibody recognizes the same epitope that antibody 266 recognizes or competes with antibody 266 for binding to soluble Aβ.

12. **(Original)** The method of any one of Claims 1 - 11, wherein the affinity is measured with respect to either Aβ1 - 40 or Aβ1 - 42.

13. **(Original)** The method of any one of Claims 1 - 12, additionally comprising measuring cognition in the subject before administering the antibody

14. **(Original)** The method of Claim 13, additionally comprising measuring cognition in the subject after administering the antibody.

15. **(Original)** The method of Claim 14, wherein the measure of cognition after administering the antibody shows a significant improvement in cognition compared with the measure of cognition before administering the antibody.

16. **(Original)** The method of any one of Claims 1 - 15, additionally comprising measuring cognition in the subject after administrating the antibody.

17. **(Original)** The use of an anti-Aβ antibody to prepare a medicament for any one of the methods of Claims 1 - 16.

18. **(New)** An isolated nucleic acid molecule encoding a humanized immunoglobulin light chain, or variable region thereof, the light chain or variable region comprising:

(a) three variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and

(b) a variable region framework from a human acceptor immunoglobulin light chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(i) a residue that non-covalently binds antigen directly;

(ii) a residue adjacent to a CDR;

(iii) a CDR-interacting residue; and

(iv) a residue participating in the VL-VH interface.

19. (New) An isolated nucleic acid molecule encoding a humanized immunoglobulin heavy chain, or variable region thereof, the heavy chain or variable region comprising:

(a) three variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4, and

(b) a variable region framework from a human acceptor immunoglobulin heavy chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(i) a residue that non-covalently binds antigen directly;

(ii) a residue adjacent to a CDR;

(iii) a CDR-interacting residue; and

(iv) a residue participating in the VL-VH interface.

20. (New) An isolated nucleic acid molecule encoding a humanized immunoglobulin light chain, or variable region thereof, the light chain or variable region comprising:

(i) three light chain complementarily determining regions (CDRs) from the mouse monoclonal antibody 3D6, wherein the light chain CDRs have the following amino acid sequences:

light chain CDR1:
Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn (residues 24-39 of SEQ ID NO:2);

light chain CDR2:
Leu Val Ser Lys Leu Asp Ser (residues 55-61 of SEQ ID NO:2); and

light chain CDR3:
Trp Gln Gly Thr His Phe Pro Arg Thr (residues 94-102 of SEQ ID NO:2); and

(ii) a light chain variable region framework sequence from a human immunoglobulin light chain, provided that at least one framework residue is substituted with the corresponding amino

acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(a) a residue that non-covalently binds antigen directly;

(b) a residue adjacent to a CDR;

(c) a CDR-interacting residue; and

(d) a residue participating in the VL-VH interface.

21. (New) An isolated nucleic acid molecule encoding a humanized immunoglobulin heavy chain, or variable region thereof, the heavy chain or variable region comprising:

(i) three heavy chain complementarily determining regions (CDRs) from the mouse monoclonal antibody 3D6:

heavy chain CDR1:
Asn Tyr Gly Met Ser (residues 31-35 of SEQ ID NO:4)

heavy chain CDR2:
Ser Ile Arg Ser Gly Gly Gly Arg Thr Tyr Tyr Ser Asp Asn Val Lys Gly (residues 50-66 of SEQ ID NO:4) and,

heavy chain CDR3:
Tyr Asp His Tyr Ser Gly Ser Ser Asp Tyr (residues 99-107 of SEQ ID NO:4); and

(ii) a heavy chain variable region framework sequence from a human immunoglobulin heavy chain, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(a) a residue that non-covalently binds antigen directly;

(b) a residue adjacent to a CDR;

(c) a CDR-interacting residue; and

(d) a residue participating in the VL-VH interface.

22. (New) The isolated nucleic acid molecule of claim 18 or 20, wherein at least one rare human light chain framework residue is substituted with an amino acid residue which is common for human variable light chain sequences at that position.

23. (New) The isolated nucleic acid molecule of claim 19 or 21, wherein at least one rare human heavy chain framework residue is substituted with an amino acid residue which is common for human variable heavy chain sequences at that position.

24. (New) A vector comprising the nucleic acid molecule of claim 18 or 20.

25. (New) The vector of claim 24, further comprising a nucleic acid molecule encoding a humanized immunoglobulin heavy chain, or variable region thereof, said heavy chain or variable region comprising at least one complementarity determining region (CDR) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4.

26. (New) A vector comprising the nucleic acid molecule of claim 19 or 21.

27. (New) The vector of claim 26, further comprising a nucleic acid molecule encoding a humanized immunoglobulin light chain, or variable region thereof, said light chain or variable region comprising at least one complementarity determining region (CDR) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2.

28. (New) A host cell comprising a first expression vector, said first expression vector comprising the nucleic acid molecule of claim 18.

29. (New) The host cell of claim 28, further comprising a second expression vector, said second expression vector comprising a nucleic acid molecule encoding a humanized immunoglobulin heavy chain, or variable region thereof, said heavy chain or variable region comprising at least one complementarity determining region (CDR) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4.

30. (New) The host cell of claim 28, further comprising a second expression vector, said second expression vector comprising a nucleic acid molecule encoding a humanized immunoglobulin heavy chain, or variable region thereof, said heavy chain or variable region comprising:

(a) three variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4, and

(b) a variable region framework from a human acceptor immunoglobulin heavy chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(i) a residue that non-covalently binds antigen directly;

(ii) a residue adjacent to a CDR;

(iii) a CDR-interacting residue; and

(v) a residue participating in the VL-VH interface.

31. (New) A host cell comprising a first expression vector, said first expression vector comprising the nucleic acid molecule of claim 19.

32. (New) The host cell of claim 31, further comprising a second expression vector, said second expression vector comprising a nucleic acid molecule encoding a humanized immunoglobulin light chain, or variable region thereof, said light chain or variable region comprising at least one complementarity determining region (CDR) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2.

33. (New) The host cell of claim 31, further comprising a second expression vector, said second expression vector comprising a nucleic acid molecule encoding a humanized immunoglobulin light chain, or variable region thereof, said light chain or variable region comprising:

(a) three variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and

(b) a variable region framework from a human acceptor immunoglobulin light chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(i) a residue that non-covalently binds antigen directly;

(ii) a residue adjacent to a CDR;

(iii) a CDR-interacting residue; and

(vi) a residue participating in the VL-VH interface.

34. (New) A host cell comprising an expression vector, the vector comprising:

(a) the nucleic acid molecule of claim 18; and

(b) a nucleic acid molecule encoding a humanized immunoglobulin heavy chain, or variable region thereof, said heavy chain or variable region comprising at least one complementarity determining region (CDR) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4.

35. (New) A host cell comprising a vector, the vector comprising:

(a) the nucleic acid molecule of claim 19; and

(b) a nucleic acid molecule encoding a humanized immunoglobulin light chain, or variable region thereof, said light chain or variable region comprising at least one complementarity determining region (CDR) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2.

36. (New) The host cell of any one of claims 28-35, which is a mammalian host cell.

37. (New) The host cell of claim 36, which is selected from the group consisting of a CHO cell, a COS cell, a HeLa cell, a myeloma cell, a hybridoma, or a transformed B-cell.

38. (New) A method of producing a humanized immunoglobulin, or an antigen-binding fragment thereof, comprising culturing the host cell of claims 28-35 under conditions such that the immunoglobulin or antigen-binding fragment is produced and isolating said antibody or antigen-binding fragment from the host cell or culture.

39. (New) The method of claim 38, wherein the humanized immunoglobulin or antigen-binding fragment specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^7 M^{-1}.

40. (New) The method of claim 38, wherein the antigen-binding fragment is selected from the group consisting of a Fab, a Fab', a Fabc, a Fv, a F(ab')2 fragment, and a single chain antibody.